Remarks

Applicant has carefully studied the Office Action, mailed June 3, 2009. Applicant believes the amendments appearing above and these explanatory remarks are fully responsive to the Action. Accordingly, this important patent application is now in condition for allowance.

Status of the Claims

Claims 19-20, 23-24 and 26 were pending and under consideration. Claims 20 and 24 have been canceled. Claims 19, 23 and 26 have been amended. Claim 27 is new. All amendments appearing above are supported by the original specification and figures. Therefore claims 19, 23, 26 and 27 are presented for consideration.

Claim Rejections

35 U.S.C. §112

Claims 20 and 23 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant gratefully thanks Examiner for her suggestions. Applicant has canceled claim 20. Applicant has amended claim 23 to provide sufficient antecedent basis for the limitation. Accordingly, Applicant respectfully requests that the rejection as to claims 20 and 23 be withdrawn.

Claim Rejections - 35 U.S.C. §103(a)

Claim 19

Claims 19, 20, 23, 24 and 26 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Garattini *et al.* (Current Opinion in Pharmacology) ("Garattini") in view of Bernardi *et al.* ("Bernardi"). Applicant respectfully requests favorable reconsideration and withdrawal of the

rejection on these grounds as the proposed combination does not teach all the elements of claim 19 (as amended).

Amended claim 19 recites a method of inducing apoptosis in cancer cells comprising contacting the cells with imatinib mesylate and suberoylanilide hydroxamic acid. Office notes on page 4 of the Office Action dated June 3, 2009 that neither Garattini nor Bernardi teach the administration of suberoylanilide hydroxamic acid (SAHA) in conjunction with imatinib mesylate. Office asserts on page 4 of the Office Action dated June 3, 2009 that Garattini teaches that SAHA, a histone deacetylase inhibitor (HDAC inhibitor) is endowed with apoptotic properties. However, in this reference, SAHA is not being used to promote apoptosis, but rather is being used to promote cytodifferentiation. Cytodifferentiation is a totally different concept than apoptosis. Cytodifferentiation forces neoplastic cells to acquire a phenotype that is similar to that of their corresponding terminally differentiated normal counterparts in an attempt to avoid the side effects of cytotoxic chemotherapy (page 358, col. 2; Abstract). Apoptosis, on the other hand, refers to the process of programmed cell death. The entirety of Garattini is concerned with cytodifferentiation, not apoptosis. Garattini teaches away from the use of SAHA in inducing apoptosis given that the entirety of Garattini teaches cytodifferentiation in which the cells are kept alive. Office asserts on page 7 that Garattini teaches that HDAC inhibitors such as SAHA are endowed with apoptogenic properties. The mere statement that SAHA possesses apoptotic properties without any showing in the reference of the use of SAHA in promoting apoptosis is insufficient to obviate the present application.

Office also states on page 4 of the Office Action dated June 3, 2009 that STI571 (imatinib mesylate) is a powerful c-Abl inhibitor that is in clinical trials for the treatment of chronic myelogenous leukemia. Garattini does not indicate the successful treatment of chronic myelogenous leukemia but rather merely states that the drug is in clinical trials. Given that Garattini does not teach the administration of imatinib mesylate in conjunction with SAHA, Garattini is insufficient to obviate.

Office cites Bernardi to overcome the deficiencies of Garattini. Office states on page 4 of the Office Action dated June 3, 2009 that Bernardi teaches that combinations of complementary or synergistic antitumoural drugs are often utilized in cancer therapy. However, prior to

Applicant's administration of SAHA and imatinib mesylate together, it was not known if the drugs had a synergistic effect hence there was no reason to combine them. Merely because two different drugs are each used to treat leukemia is not a sufficient motivation to combine the drugs and expect successful results. Neither Garattini nor Bernardi discuss the use of SAHA to make imatinib mesylate refractory cells more susceptible to the effects of imatinib mesylate. Bernardi states on page 3455 column 1 that SAHA can be used to treat acute promyelocytic leukemia (APL). Garattini uses SAHA as a cytodifferentiation agent. However, there is no mention of using SAHA to treat chronic myelogenous leukemia (CML) or acute lymphocytic leukemia (ALL) in either of the cited references. An express limitation of amended claim 19 is that the cancer cells treated are either CML cells or ALL cells. Given that neither Garattini nor Bernardi teach this limitation of the claim, the cited combination cannot be said to obviate.

Claim 23

Claim 23 depends from claim 19 and further recites the limitation that the cells are exposed to the imatinib mesylate and the suberoylanilide hydroxamic acid for about 48 hours. This limitation is not present in either Garattini or in Bernardi. In fact, neither reference, nor the combination of the references teaches administration of these drugs together. The combination of references similarly does not disclose exposing the cells to the drugs for about a 48 hour time period. As such, the cited combination fails to teach each and every limitation of the claim and thus cannot be said to obviate.

Claim 24 and 26

Claims 24 and 26 depend from claim 19 and further recite the limitation that the cancer cells are chronic myelogenous leukemia cells that are either accelerated-phase or blast crisis phase. The cited combination does not teach the administration of imitinib mesylate and suberoylanilide hydroxamic acid together to induce apoptosis in chronic myelogenous leukemia cells that are in accelerated-phase or blast crisis phase. As stated in the original specification at paragraph [0013] treatment with imitinib mesylate alone has been successful with cells in the chronic phase but the accelerated and blast crisis phases prove to be highly resistant to imatinib mesylate. Neither of the references, nor their combination, teach the administration of either drug to chronic myelogenous leukemia cells in accelerated or blast crisis phase. Given that the cited

combination of references fails to teach each and every limitation of the claims, the cited combination cannot be said to obviate.

For these reasons at least, Applicant requests the reconsideration and withdrawal of the rejection of claim 19 under 35 U.S.C. §103(a). Likewise, all remaining claims depend from claim 19 and are also nonobvious under 35 U.S.C. §103(a).

Conclusion

Entry of a Notice of Allowance is solicited. If the Office is not fully persuaded as to the merits of Applicant's position, or if an Examiner's Amendment would place the pending claims in condition for allowance, a telephone call to the undersigned at (813) 925-8505 is requested.

Very respectfully,

SMITH & HOPEN

/michele l lawson/

By:_____

Dated: September 3, 2009

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CERTIFICATE OF ELECTRONIC TRANSMISSION

(37 C.F.R. 2.190 (b))

I HEREBY CERTIFY that this correspondence is being electronically transmitted to the Patent and Trademark Office through EFS Web on September 3, 2009.

/lauren reeves/

Date: September 3, 2009

Lauren Reeves